

We claim:

1. A targeting construct comprising:
 - (a) a first polynucleotide sequence homologous to a 5-HT-2B gene;
 - 5 (b) a second polynucleotide sequence homologous to the 5-HT-2B gene; and
 - (c) a selectable marker.
2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
3. A method of producing a targeting construct, the method comprising:
 - 10 (a) providing a first polynucleotide sequence homologous to a 5-HT-2B gene;
 - (b) providing a second polynucleotide sequence homologous to the 5-HT-2B ;
 - (c) providing a selectable marker; and
 - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
- 15 4. A method of producing a targeting construct, the method comprising:
 - (a) providing a polynucleotide comprising a first sequence homologous to a first region of a 5-HT-2B gene and a second sequence homologous to a second region of a 5-HT-2B gene;
 - (b) inserting a positive selection marker in between the first and second sequences
 - 20 to form the targeting construct.
5. A cell comprising a disruption in a 5-HT-2B gene.
6. The cell of claim 5, wherein the cell is a murine cell.
7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.
8. A non-human transgenic animal comprising a disruption in a 5-HT-2B gene.
- 25 9. A cell derived from the non-human transgenic animal of claim 8.
10. A method of producing a transgenic mouse comprising a disruption in a 5-HT-2B gene, the method comprising:
 - (a) introducing the targeting construct of claim 1 into a cell;
 - (b) introducing the cell into a blastocyst;
 - 30 (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

- (d) breeding the chimeric mouse to produce the transgenic mouse.
11. A method of identifying an agent that modulates the expression of a 5-HT-2B, the method comprising:
 - (a) providing a non-human transgenic animal comprising a disruption in a 5-HT-2B gene;
 - (b) administering an agent to the non-human transgenic animal; and
 - (c) determining whether the expression of 5-HT-2B in the non-human transgenic animal is modulated.
 12. A method of identifying an agent that modulates the function of a 5-HT-2B, the method comprising:
 - (a) providing a non-human transgenic animal comprising a disruption in a 5-HT-2B gene;
 - (b) administering an agent to the non-human transgenic animal; and
 - (c) determining whether the function of the disrupted 5-HT-2B gene in the non-human transgenic animal is modulated.
 13. A method of identifying an agent that modulates the expression of 5-HT-2B, the method comprising:
 - (a) providing a cell comprising a disruption in a 5-HT-2B gene;
 - (b) contacting the cell with an agent; and
 - (c) determining whether expression of the 5-HT-2B is modulated.
 14. A method of identifying an agent that modulates the function of a 5-HT-2B gene, the method comprising:
 - (a) providing a cell comprising a disruption in a 5-HT-2B gene;
 - (b) contacting the cell with an agent; and
 - (c) determining whether the function of the 5-HT-2B gene is modulated.
 15. The method of claim 13 or claim 14, wherein the cell is derived from the non-human transgenic animal of claim 8.
 16. An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.
 17. A transgenic mouse comprising a disruption in a 5-HT-2B gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: embryonic lethality, abnormal embryos, retarded development, and reabsorbed embryos.

Abstract